

Prior to initiating the testing of a substance, an NIEHS/NTP staff scientist develops a research concept document. This research concept outlines the general elements for a program of study of the substance to address specific research needs raised in its nomination to the testing program.

Additional information about the nomination, review, and selection of substances for study by the NTP is provided from *Nominations to the NTP Testing Program*
<http://ntp.niehs.nih.gov/go/nom>

NTP Concept Document: N-Butyl Glycidyl Ether

Background

n-BGE is a high production volume industrial chemical used as a diluent or chemical intermediate in epoxy resins which are widely used in electronics, construction, and coating materials. Humans are exposed to n-BGE in workplace via inhalation, ingestion, or skin or eye contact.

n-BGE is mutagenic in Salmonella TA97, TA100, TA1535 with or without S9, but not in the frameshift strain TA98. It induces DNA repair in human peripheral blood lymphocytes and W138 cells in vitro. Intraperitoneal administering of n-BGE induced increase in micronuclei in mice and chromosomal aberrations in bone marrow cells in rats. In reproductive studies in mice, n-BGE induced dominant lethal effects, decreased pregnancy rates, and increased fetal deaths.

n-BGE was nominated for general toxicity, reproductive toxicity, and carcinogenicity studies because of potential human exposure, structural features, and lack of toxicity data.

Hypothesis

n-BGE is suspected to be carcinogenic based on its chemical structure, known mutagenicity, and its known interaction with nucleosides and DNA.

Proposed Research Project

n-BGE has been on the EPA's master testing list and is a chemical submitted to the EPA's High Production Volume Chemical Challenge program by the Society of the Plastics Industry, Inc. and the Epoxy Resin Systems Task Group. The NTP Office of Nominations & Selections has provided all the documents and communications obtained from EPA officials on n-BGE. No further input from EPA is expected at this point. The following preliminary research projects proposed are based on the understanding of the interests and ideas of the EPA officials, of a representative of the Society of the Plastics Industry and the Epoxy Resin Systems Task Group, and of NIEHS scientists.

i 14-Day, 90-day, and 2-year inhalation exposure studies in rats and mice. The SMVCE (Sperm motility and vaginal cytology) is performed in 90-day study animals and this serves as a screen for reproductive toxicity. If the results of SMVCE are suggestive of possible reproductive

toxicity then a separate definitive study will be designed and performed.

ii ADME studies including identification of the active metabolite(s) and toxicokinetics, DNA adduct formation, changes in gene expression, mutation frequency of oncogenes in mouse lung tumors.

iii Micronuclei formation in 90-day study animals. Chromosomal aberrations in rat bone marrow cells will be considered during the design of studies.

iv DNA damage analysis (Comet test) in lung and liver tissues and in blood leukocytes. .

Specific Aims

The main objective of these studies is to characterize toxicity and carcinogenicity of n-BGE in rats and mice by whole body inhalation exposure. Proposed determination of DNA-adduct levels, evaluation of changes in gene expression by microarray and gene mutation frequencies in the lung tumors may help in understanding the mechanism of toxicity/carcinogenicity for this chemical.

Significance

The results of proposed studies would contribute to the information needed for overall risk assessment of n-BGE exposure to humans.

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